

In the Specification

At pages 61-63, please amend the following paragraphs as follows:

This Example describes the construction and expression of a modified gp120-CD4 chimeric polypeptide having an immunoglobulin polypeptide sequence, ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1. This exemplary heterologous domain adds functionality to the gp120-CD4 chimeric polypeptide, including adhesin and immunopotentiating functions, prolonging stability, increasing circulating half-life and ability to cross the placental barrier. This example also shows that the ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 chimera binds to co-receptor expressed on the surface of intact cells and neutralizes HIV virus. Gp120, a subunit of the envelope protein of HIV-1 binds to CD4 and undergoes a conformational change that permits the complex to interact with a co-receptor, such as CCR5. This interaction permits the infection of HIV-1 into target CD4+ cells. Antibodies or other agents that interfere with the interaction of HIV-1 with the co-receptor can prevent infection.

To identify such agents, ~~single chain gp120-CD4~~ FLSC R/T-IgG1 was modified by fusion to the constant regions that form the IgG1 heavy chain, hinge CH2 and CH3 (FIG. 9). ~~Gp120-CD4-IgG1~~ FLSC R/T-IgG1 can be used to identify agents that block, inhibit, or disrupt HIV-1 interaction with the co-receptor, thereby identifying agents that inhibit HIV infection. The ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 polypeptide comprising SEQ ID NOs: ~~30 24~~, 11, 26 and 32 could also be used as a passive immunotherapeutic to prevent HIV infection after an acute exposure, such as a needlestick injury.

Two hundred ninety-three cells were transiently transfected with the plasmid containing ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 comprising at least SEQ ID NOs: ~~29 23~~, 25 and 31, and the expressed protein was characterized by immunoblotting of the culture supernatants. Briefly, collected supernatant samples were electrophoresed onto a 4-20% gradient PAGE gel. Fractionated proteins were transferred to nitrocellulose and detected with a mixture of anti-gp120 monoclonal antibodies. As shown in FIG. 10, the transiently transfected cells expressed ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 (lane 1). Supernatant from cells expressing purified gp120 derived from HIV-1 BaL (lane 2) was electrophoresed for relative size comparison. The ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 polynucleotide encodes a protein having the predicted size for a ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 heavy-chain chimera. Like the original gp120-CD4, a portion of ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 is cleaved producing a 120 kDa protein fragment that is most likely gp120 ("Cleaved gp120"). The size of this fragment suggests that ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 is being cleaved within the spacer. To assure that the ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1

is folded into a conformation permissive for binding co-receptor, dilutions of the supernatant were added to L 1.2 cells that express either CCR5 or CXCR4 co-receptors. Bound ~~gp120-CD4-IgG1~~ FLSC R/T-IgG1 was detected with anti-human IgG that was labeled with Europium, a fluorescent reagent. The amount of fluorescence is directly related to the amount of bound material.